

## **REMARKS**

### **I. Introduction**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following reasons.

### **II. Summary of the Claims and Amendments to the Application**

In the specification, the Brief Description of the Drawings has been amended to specifically identify those regions of sequence homology that are claimed in claims 49-51. MPEP § 2422.02. This section also has been amended to include sequence identifiers.

Claims 1-55 are pending in this application. Claims 41-45, 47 and 48 have been withdrawn from consideration by the PTO in view of the Restriction Requirement, which has been made final. Claims 8, 9 and 19, and 49-51 have been amended.

Claim 8 has been amended to insert a missing hyphen in the second line of item (e) and to correct a typographical error made in the previous amendment, which was identified by the PTO.

Claim 9 has been amended to clarify that variable X in formula (I) encompasses all possible natural amino acids as well as the non-conventional amino acids set forth in Table 2 (see specification at page 27 *et seq*).

Claim 19 has been amended to insert a missing space between the word “the” and the letter “Z” in the first line of that claim.

Claims 9 and 49-51 also have been amended to include sequence identifiers in compliance with the sequence rules.

For the foregoing reasons, the amendments made herein are fully supported by the specification and do not include new matter. Accordingly, entry of the amendments is respectfully solicited.

### **III. The Office Action**

Applicants gratefully acknowledge the PTO's withdrawing the anticipation rejections based on Masci et al., WO 99/58569 ("Masci") and Willmott et al., *Fibrinolysis*, 9:1-8 (1995) ("Willmott"). The Office Action raised new rejections, to which Applicants now turn in the order presented.

#### **A. Objection to the Claims**

The PTO objected to claim 8 because the previous amendment erroneously struck through item (f), which should have been maintained. Office Action at page 2. Applicants respectfully submit that the amendments to the claims have mooted this objection.

#### **B. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph**

Claims 1-40, 46 and 49-55 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement because the specification supposedly indicates unpredictability in the *in vivo* assay results as to alleviation of blood loss. *Id.* Specifically, the PTO concluded that Applicants' disclosure "indicates unpredictability of its own data . . ." *Id.* Applicants respectfully traverse this ground for rejection.

The PTO appears to have misread the specification (*i.e.*, page 50, lines 1-14), which states that the *comparisons* of assay results, rather than the results themselves, may warrant "further scrutiny." Thus, Applicants' results exemplify and therefore enable the use of the claimed plasmin inhibitor, specifically for *in vivo* alleviation of blood loss. As such, the claimed invention fully satisfies the enablement requirement and Applicants respectfully urge the PTO, therefore, to reconsider and withdraw this rejection.

#### **C. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph**

Claims 9 and 49-51 stand rejected under 35 U.S.C. § 112, second paragraph, for being allegedly indefinite because the rejected claims do not comply with the sequence rules (MPEP § 2422.03). Office Action at page 3. In response, Applicants have submitted a revised sequence listing to identify the generic sequence in claim 9 and those specific regions of

sequence homology that are claimed in claims 49-51. These amendments, together with the amendment to the Brief Description of the Drawings noted above, should moot this ground for rejection.

The PTO rejected claim 9 for indefiniteness on account of the claim reciting "X is any amino acid." Applicants amended the claim to explicitly recite the naturally-occurring amino acids as well as the non-conventional amino acids described in the specification at pages 27-28 (Table 2). The claim distinctly claims and particularly points out the claimed subject matter, and that the rejection therefore should be reconsidered and withdrawn.

**D. Rejection of Claims Under 35 U.S.C. § 103(a)**

Claims 1-7 were rejected under 35 U.S.C. § 103(a) for being allegedly unpatentable over previously cited Willmott. In particular, the PTO alleged that it would have been obvious to one of ordinary skill in the art at the time that the claimed invention was made to further purify the bioactive single stage competitive plasmin inhibitor beneficially taught by Willmott. The PTO suggested that some of the advantages of such purification is that the purified peptides would be more storage-stable; generally exhibit an increased specific activity; be amenable to amino acid sequencing which can lead to recombinant means of enzyme production with its accompanying savings and costs; and allow for ready separation of reaction products as compared to separations which must account for impurities. Applicants respectfully traverse this ground for rejection.

Willmott does not render the claims obvious for at least the reason that the reference would not have motivated a skilled person to further purify the disclosed plasmin inhibitor preparation.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

MPEP § 2143.01 (v. 8, rev. 2, May 2004).

Willmott repeatedly teaches a plasmin inhibitor preparation that consists of “a single 7 kDa protein, as assessed by SDS-PAGE and staining with Coomassie blue R250.” *See, e.g.*, Willmott at page 5 (emphasis added). By contrast to the PTO’s urgings, there is no suggestion whatsoever in Willmott that the plasmin inhibitor preparation is a “partially-purified bioactive peptide” that could give rise to the advantages noted above if only a skilled person purified the preparation. A person of skill in the art would have understood that the disclosed plasmin inhibitor preparation was already sufficiently pure, and therefore would have had no motivation at all to purify the preparation of Willmott to arrive at the claimed invention.

The rejection turns impermissibly upon Applicants’ own disclosure that the preparation taught by Willmott contains a mixture of plasmin inhibitors. That is to say, absent the benefit of Applicants’ invention, a person of skill would not have known that the plasmin inhibitor preparation in the putative prior art was in fact an impure mixture.

It is well-settled law that “[a]ny judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and *does not include knowledge gleaned only from applicant’s disclosure*, such a reconstruction is proper.” *In re McLaughlin*, 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971) (emphasis added). Here, the PTO applied Applicants’ disclosure in the obviousness determination based on Willmott, and thereby fell “victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.” *In re Kotzab*, 217 F.3d 1365, 1369, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000) (citing *In re Dembiczak*, 175 F.3d 994, 998, 50 USPQ2d 1614, 1616 (Fed. Cir. 1999) (internal quotes omitted)). *See also* MPEP § 2145(X)(A). Consequently, a skilled person would not have known that the preparation of Willmott was impure as *taught only by Applicants*, and thus would have had no reason to purify the preparation. The invention therefore would not have been obvious to the skilled person. Accordingly, Applicants respectfully request the PTO to reconsider and withdraw this rejection.

**IV. Conclusion**

This application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if he feels that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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By



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**The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.**